CHAPTER 1.1

Documentation in Pharmaceutical Industry

1.1.1 Master Formula Record - Definition

"A document or set of documents describing the raw materials and quantities, as well as the procedures and precautions required to manufacture a specific quantity of a final product, as well as the processing instructions, including in-process controls." For each product and batch size to be generated, Master Formula papers referring to all production methods must be kept. These must be created and approved by qualified technical personnel, such as the head of manufacturing and quality control. MFR is a key regularity in each batch of production.

1.1.2 Master Formula Record

- A master formula record (MFR) is a document that includes all of the details about a pharmaceutical product.
- The MFR contains all information about the manufacturing process of the product.
- The MFR is prepared by the company's research and development staff.
- When establishing batch manufacturing records, manufacturing units use MFR as a reference standard (BMR).
- Master Manufacturing Record, often known as MFR, is a type of manufacturing record.

1.1.3 MFR - Product Details

- ✓ Name, logo and address of the manufacturing company.
- ✓ Dosage form name.
- ✓ Brand name.

- ✓ Generic name.
- ✓ Product code
- ✓ Label claim of all ingredients
- ✓ Product description and quality of raw materials
- ✓ Batch size
- ✓ Pack size and packing style
- ✓ Shelf life
- ✓ Storage conditions
- ✓ MFR number and date
- ✓ Supersede MFR number and date
- ✓ Effective batch number
- ✓ Authorization by the production and quality assurance head

Flow Chart: The steps that will be tracked in the manufacturing process. Material flow from dispensing to final product distribution to stores is depicted in this flowchart.

Equipment: Make a list of all the necessary equipment and machines for the production process, along with their capacities.

Special instructions: Make a list of any precautions or special instructions that must be followed during the product's manufacturing and packaging, and include them in the batch manufacturing formula.

Calculations: To acquire 100 percent of the active ingredient, include the calculation procedures for all active materials. To reach 100 percent potency, the calculation should be done with water or LOD.

Manufacturing Process: Every stage of the manufacturing process must be recorded. Shifting, milling, lubrication, granulation, compression, and coating should all be meticulously documented, as should the process duration and yield. For each phase, it also incorporates environmental parameters such as temperature, humidity, and storage conditions.

Packing Process: All packing materials, as well as their quantities, are listed. The details should include line clearance and reconciliation of printed and unprinted packing goods.

Include the batch's theoretical, real, and acceptable constraints in the yield.

1.1.4 Procedure to Prepare a Master Formula Record

The knowledge of seasoned specialists, such as manufacturing or analytical chemists, is combined with the manufacturing history of a batch size to create a Master Formula Record. At any level, we cannot overlook the Master formula record.

All prior and new employees are then handed the Master Formula Record. In batch processing, it's a common document. The Master Formula record is the gold standard when it comes to creating a Batch Manufacturing Record.

1.1.5 SOP for Preparation of the Master Formula Record

RESPONSIBLE DEPARTMENTS:

Primary Responsibility:

F&D and Production Department

Secondary Responsibility:

Quality Assurance Department

ACCOUNTABILITY:

Head-Quality Assurance shall be responsible for Implementation of SOP.

1.1.6 Steps to Prepare a Master Formula Record

- Production Department in association with F&D shall prepare MFR.
- MFR shall prepare as per the format attached with this SOP.
- MFR shall be divided into two parts:
- Packaging part
- Manufacturing part

1.1.7 The First Page of both the Sections Shall have Following Details

- Name, address and logo of the company
- Dosage form
- Brand name
- Generic name

- Product code
- Label claim: This should include all ingredients and text included in product permission
- Product Description
- Batch Size
- Pack Size
- Shelf Life
- Storage conditions
- Drug Schedule: whether schedule H or schedule G drug.
- Superseded Master card number and Date.
- Present Master card number and Date.
- Present Master card effective Batch number.
- Reference of changed control number.
- There shall be authorization of Master Formula Record by all the responsible members
- The secondary page of manufacturing section shall include-Process steps to be monitored.
- Subsequent pages shall include the processes to be monitored. The stage wise movement of material in a form of flow chart.
- The list of equipment, machines, utensils to be used, shall be described.
- Any particular measures to be taken for the product during manufacture and packing will be listed on the next page. Batch Manufacturing Formula should be included on the same page.

1.1.8 Batch Formula should have the following columns

- Serial number
- Name of ingredients
- Reference of specifications of ingredients
- Quantity to be added (in mg/ml or per tablet or per capsule or per gm. as the case may be)
- Overages to be added (in %)
- Quantity to be added per batch or per lot below that give the calculation step for every active

- Material, ensuring that the active material shall be compensated for assay values less than 100% which could be due to less potency or higher moisture content.

1.1.9 At the End of Every Important Stage, include a Statement of the Yield with the Acceptable Limits

Include quality checks at the beginning and end of essential processes and stages, as well as at the process's boundaries.

The tools that will be utilised must be included in the technique. Methods or references to methods/procedures for preparing, cleaning, assembling, and operating diverse equipment must be provided.

Include clear, step-by-step directions for processing (example: checks on materials, pretreatments, sequence for adding materials, mixing times, temperatures, humidity etc.)

Product storage conditions must meet certain criteria.

1.1.10 The Packaging Part of MFR

Check for line clearance during batch coding and batch packaging activities.

Includes appropriate packaging element reconciliation (printed and unprinted).

Extra or rejected and printed packaging materials are discarded.

Describes the packing operation, as well as any relevant supporting operations and equipment.

Master Formulation Record

Isopropyl alcohol antiseptic 75% topical solution			
Name:	**isopropyl alcohol**	**Batch Volume:**	50,000 mL (50 L)
Concentration:	75%	**Dispensed Product:**	50 mL or 1,000 mL
Route:	Topical	**Beyond-Use Date:**	1-year
Form:	Solution	**Storage:**	Room Temperature
Auxiliary Labeling:	Flammable, external use only, avoid contact with eyes		

INGREDIENTS	AMOUNT	FINAL CONCENTRATION
Isopropyl alcohol 99.8%, USP	37,575 mL	75% (v/v) *(active ingredient)*
Hydrogen peroxide 3%, USP	2,085 mL	0.125% (v/v)
Glycerin 98%, USP	725 mL	1.45% (v/v)
Sterile Water for Irrigation, USP	~9,615 mL	*(qs to final volume)*
Total Batch Volume:	**50,000 mL**	

EQUIPMENT AND SUPPLIES
15-gallon stainless steel pot w/ spigot and fitted lid with opening
Large plastic stir
1,000 mL graduated cylinder
500 mL graduated cylinder
250 mL graduated conical beaker
Silicone adapter for dispenser
50 mL plastic bottle with flip top dispensing lid
1,000 mL plastic bottle with spray apparatus
PPE: R-95 mask, lab goggles, gown, gloves

LABEL

METHOD OF PREPARATION

Note: Preparation to occur only in the negative pressure nonsterile compounding room. PPE required during preparation. Remove any sources of potential flame or spark to minimize fire risk.

1. Measure quantities of isopropyl alcohol and hydrogen peroxide in separate graduated cylinders and combine them in a 15-gallon stainless steel pot.
2. Measure glycerin in a conical graduated cylinder and add to mixture in stainless steel pot. As glycerin is very viscous and sticks to the wall of the measuring cylinder, it should be rinsed with some sterile water for irrigation and then emptied into the kettle.
3. Measure quantities of sterile water for irrigation sufficient to final volume of 50,000 mL and add to the mixture in the pot.
4. Carefully stir solution in kettle and place stainless steel lid on kettle to minimize vapors while dispensing.
5. Using stainless steel spigot and empty plastic bottle, slowly open flow to fill 1,000 mL empty plastic bottle to approximately 1,000 mL.
6. Product can further be unit dosed into either: (1) 50 mL bottles with dispensing lid, or (2) 1,000 mL spray bottle.

FINAL PRODUCT DESCRIPTION / QUALITY ASSURANCE

- Clear colorless low viscosity liquid
- Verify final alcohol concentration of hand sanitizer using an alcohol meter. Isopropyl 75% will be shown as 77% (+/- 1%) on the scale.
- Due to the high alcohol content of this formula, it is considered self-preserved. Filled, bottles should be quarantined for 72-hours to eliminate any spores present.

REFERENCES

1. World Health Organization. (2010). Guide to local production: WHO-recommended hand rub formulations. Geneva: WHO.
2. Food and Drug Administration (FDA) – Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency. March 2020.

Figure 1

References

1. A Textbook of Pharmaceutical Quality assurance by Mr. Sanjay A. Nagdev, Mr. Mayur R. Bhurat, Dr. Md. Rageeb Md. Usman Dr. Krishna R. Gupta, Dr. Upendra B. Gandagule.
2. https://www.slideshare.net/NavaneethakrishnanPa4/documentation-in-pharmaceutical-industry-144312056.